

We claim:

1. An isolated human monoclonal antibody which binds to human CD20.
2. The antibody of claim 1, selected from the group consisting of an IgG1, an IgG2, an IgG3, an IgG4, an IgM, an IgA1, an IgA2, a secretory IgA, an IgD, and an IgE antibody.
3. The antibody of claim 2, wherein the antibody is an IgG1 antibody.
4. The antibody of claim 2, wherein the antibody is an IgG3 antibody.
5. The antibody of claim 2, wherein the antibody is an IgG4 antibody.
6. The antibody of claim 2, wherein the antibody is an IgA1 or IgA2 antibody.
7. The antibody of claim 1, wherein the antibody dissociates from human CD20 with a dissociation rate constant (k_d) of about 10^{-5} sec^{-1} or less.
8. The antibody of claim 1, wherein the antibody binds to human CD20 with an affinity constant (K_D) of about 5 nM or less.

9. The antibody of claim 1, wherein the antibody has one or more of the characteristics selected from the group consisting of:

(I) capable of inducing complement dependent cytotoxicity (CDC) of cells expressing CD20 in the presence of complement;

5 (ii) capable of inducing complement dependent cytotoxicity (CDC) of cells expressing CD20 and high levels of CD55 in the presence of complement;

(iii) capable of inducing complement dependent cytotoxicity (CDC) of cells expressing CD20 and high levels of CD59 in the presence of complement;

(iv) capable of inducing apoptosis of cells expressing CD20;

10 (v) capable of inducing antibody dependent cellular cytotoxicity (ADCC) of cells expressing CD20 in the presence of effector cells;

(vi) capable of inducing homotypic adhesion of cells which express CD20;

(vii) capable of translocating into lipid rafts upon binding to CD20;

15 (viii) capable of prolonging the survival of a subject having tumor cells which express CD20;

(ix) capable of depleting cells expressing CD20; and

(x) capable of depleting cells expressing low levels of CD20 (CD20^{low} cells).

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10. The antibody of claim 9, which has one or more of the following characteristics selected from the group consisting of:

(i) capable of inducing at least 20% CDC mediated lysis of B-CLL cells in the presence of 33 vol/vol% plasma within 3 hours at 37 °C at an antibody concentration of 10 µg/ml;

25 (ii) capable of inducing at least 20% lysis of B-CLL cells in the presence of 33 vol/vol% whole blood cells within 3 hours at 37 °C at an antibody concentration of 10 µg/ml;

30 (iii) capable of prolonging the 50% survival rate of SCID mice injected with Daudi cells by more than 30% at a dose of 20 µg; and

(iv) capable of depleting peripheral B cells expressing low levels of CD20 (CD20^{low} B cells) to undetectable levels for more than 50 days in cynomolgus monkeys at a dosage of 6.25 mg/kg per day for 4 consecutive days.

35 11. The antibody of claim 10, which is capable of inducing at least 20% CDC mediated lysis of B-CLL cells in the presence of 33 vol/vol% plasma within 3 hours at 37 °C at an anti-CD20 antibody concentration of 10 µg/ml.

12. The antibody of claim 1 encoded by human heavy chain and human kappa light chain nucleic acids comprising nucleotide sequences in their variable regions as set forth in SEQ ID NO:1 and SEQ ID NO:3, respectively, and conservative sequence modifications thereof.

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13. The antibody of claim 1 encoded by human heavy chain and human kappa light chain nucleic acids comprising nucleotide sequences in their variable regions as set forth in SEQ ID NO:5 and SEQ ID NO:7, respectively, and conservative sequence modifications thereof.

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14. The antibody of claim 1 encoded by human heavy chain and human kappa light chain nucleic acids comprising nucleotide sequences in their variable regions as set forth in SEQ ID NO:9 and SEQ ID NO:11, respectively, and conservative sequence modifications thereof.

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15. The antibody of claim 1 having a human heavy chain and human kappa light chain variable regions comprising the amino acid sequences as set forth in SEQ ID NO:2 and SEQ ID NO:4, respectively, and conservative sequence modifications thereof.

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16. The antibody of claim 1 having human heavy chain and human kappa light chain variable regions which are at least 90% homologous to the amino acid sequences as set forth in SEQ ID NO:2 and SEQ ID NO:4, respectively.

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17. The antibody of claim 1 having a human heavy chain and human kappa light chain variable regions comprising the amino acid sequences as set forth in SEQ ID NO:6 and SEQ ID NO:8, respectively, and conservative sequence modifications thereof.

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18. The antibody of claim 1 having human heavy chain and human kappa light chain variable regions which are at least 90% homologous to the amino acid sequences as set forth in SEQ ID NO:6 and SEQ ID NO:8, respectively.

19. The antibody of claim 1 having a human heavy chain and human kappa light chain variable regions comprising the amino acid sequences as set forth in SEQ ID NO:10 and SEQ ID NO:12, respectively, and conservative sequence modifications thereof.

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20. The antibody of claim 1 having human heavy chain and human kappa light chain variable regions which are at least 90% homologous to the amino acid sequences as set forth in SEQ ID NO:10 and SEQ ID NO:12, respectively.

5 21. The antibody of claim 1 comprising at least one human variable region selected from the group consisting of:

(i) SEQ ID NOs:2, 4, 6, 8, 10, or 12; and

(ii) a sequence which is at least 90% homologous to any one of the amino acid sequences as set forth in (i) above.

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22. An isolated human monoclonal antibody which binds to an epitope on human CD20 defined by the antibody of claim 15.

15 23. An isolated human monoclonal antibody which binds to an epitope on CD20

(i) which does not comprise or require the amino acid residue proline at position 172;

(ii) which does not comprise or require the amino acid residues alanine at position 170 or proline at position 172;

20 (iii) which comprises or requires the amino acid residues asparagine at position 163 and asparagine at position 166;

(iv) which does not comprise or require the amino acid residue proline at position 172, but which comprises or requires the amino acid residues asparagine at position 163 and asparagine at position 166; or

25 (v) which does not comprise or require the amino acid residues alanine at position 170 or proline at position 172, but which comprises or requires the amino acid residues asparagine at position 163 and asparagine at position 166.

24. An isolated human monoclonal antibody which binds to CD20, wherein the antibody has one or more of the following characteristics:

(i) binds to mutant P172S CD20 (proline at position 172 mutated to serine) with at least the same affinity as to human CD20;

5 (ii) binds to mutant AxP (alanine at position 170 mutated to serine, and proline at position 172 mutated to serine) with at least the same affinity as to human CD20;

(iii) shows a reduced binding of 50% or more to mutant N166D (asparagine at position 166 mutated to aspartic acid) compared to human CD20 at an
10 antibody concentration of 10 μ g/ml; or

(iv) shows a reduced binding of 50% or more to mutant N163D (asparagine at position 163 mutated to aspartic acid) compared to human CD20 at an antibody concentration of 10 μ g/ml.

15 25. An isolated human monoclonal antibody which binds to an epitope in the small first extracellular loop of human CD20.

26. An isolated human monoclonal antibody which binds to a discontinuous epitope on CD20.
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27. An isolated human monoclonal antibody which binds to a discontinuous epitope on CD20, wherein the epitope comprises part of the first small extracellular loop and part of the second extracellular loop.

25 28. An isolated human monoclonal antibody which binds to a discontinuous epitope on CD20, wherein the epitope has residues AGIYAP of the small first extracellular loop and residues MESLNFIRAHTPYI of the second extracellular loop.

30 29. An isolated human monoclonal antibody which has the binding characteristics of the antibody of claim 15.

30. An isolated human monoclonal antibody which binds to human CD20 comprising at least one CDR sequence selected from the group consisting of:

- (i) SEQ ID NOs: 13, 14, 15, 16, 17, or 18;
- (ii) conservative sequence modifications of the sequences listed in (i);

5 and

(iii) fragments of any one of the sequences defined in (i) or (ii) which retain the ability to bind to human CD20.

31. The antibody of claim 30, comprising SEQ ID NO:15.

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32. The antibody of claim 30, comprising at least four CDR sequences selected from the group consisting of:

- (i) SEQ ID NOs: 13, 14, 15, 16, 17, or 18;
- (ii) conservative sequence modifications of the sequences listed in (i);

15 and

(iii) fragments of any one of the sequences defined in (i) or (ii) which retain the ability to bind to human CD20.

33. The antibody of claim 30, comprising SEQ ID NOs: 13, 14, 15, 16, 17, and 18.

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34. An isolated human monoclonal antibody which binds to human CD20 comprising at least one CDR sequence selected from the group consisting of:

- (i) SEQ ID NOs: 19, 20, 21, 22, 23, or 24;
- (ii) conservative sequence modifications of the sequences listed in (i);

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and

(iii) fragments of any one of the sequences defined in (i) or (ii) which retain the ability to bind to human CD20.

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35. The antibody of claim 34, comprising at least four CDR sequences selected from the group consisting of:

- (i) SEQ ID NOs: 19, 20, 21, 22, 23, or 24;
- (ii) conservative sequence modifications of the sequences listed in (i);

35 and

(iii) fragments of any one of the sequences defined in (i) or (ii) which retain the ability to bind to human CD20.

36. The antibody of claim 34, comprising SEQ ID NOs: 19, 20, 21, 22, 23, and 24.

37. An isolated human monoclonal antibody which binds to human
5 CD20 comprising at least one CDR sequence selected from the group consisting of:
(i) SEQ ID NOs: 25, 26, 27, 28, 29, or 30;
(ii) conservative sequence modifications of the sequences listed in (i);
and
(iii) fragments of any one of the sequences defined in (i) or (ii) which
10 retain the ability to bind to human CD20.

38. The antibody of claim 37, comprising SEQ ID NO:27.

39. The antibody of claim 37, comprising at least four CDR
15 sequences selected from the group consisting of:
(i) SEQ ID NOs: 25, 26, 27, 28, 29, or 30;
(ii) conservative sequence modifications of the sequences listed in (i);
and
(iii) fragments of any one of the sequences defined in (i) or (ii) which
20 retain the ability to bind to human CD20.

40. The antibody of claim 39, comprising SEQ ID NOs: 25, 26, 27, 28, 29, and 30.

41. The antibody of claim 1 comprising at least one CDR selected
from the group consisting of
(i) SEQ ID NOs:13, 19, or 25, or a sequence having 1 amino acid
substitution, deletion or addition of the sequence of SEQ ID NOs:13, 19 or 25;
(ii) SEQ ID NOs:14, 20, or 26, or a sequence having 1-4 amino acid
30 substitutions, deletions or additions of the sequence of SEQ ID NOs:14, 20, or 26;
(iii) SEQ ID NOs:15, or 27, or a sequence having 1-4 amino acid
substitutions, deletions or additions of the sequence of SEQ ID NOs:15, or 27;
(iv) SEQ ID NO: 16, or a sequence having 1-2 amino acid substitutions,
deletions or additions of the sequence of SEQ ID NO:16;
35 (v) SEQ ID NO: 17, or a sequence having 1-2 amino acid substitutions,
deletions or additions of the sequence of SEQ ID NO:17; and
(vi) SEQ ID NOs: 18, or 30, or a sequence having 1-2 amino acid
substitutions, deletions or additions of the sequence of SEQ ID NOs: 18, or 30.

42. The antibody of claim 41 comprising at least four CDRs selected from the group consisting of

- (i) SEQ ID NOs:13, 19, or 25, or a sequence having 1 amino acid substitution, deletion or addition of the sequence of SEQ ID NOs:13, 19 or 25;
- (ii) SEQ ID NOs:14, 20, or 26, or a sequence having 1-4 amino acid substitutions, deletions or additions of the sequence of SEQ ID NOs:14, 20, or 26;
- (iii) SEQ ID NOs:15, or 27, or a sequence having 1-4 amino acid substitutions, deletions or additions of the sequence of SEQ ID NOs:15, or 27;
- (iv) SEQ ID NO: 16, or a sequence having 1-2 amino acid substitutions, deletions or additions of the sequence of SEQ ID NO:16;
- (v) SEQ ID NO: 17, or a sequence having 1-2 amino acid substitutions, deletions or additions of the sequence of SEQ ID NO:17; and
- (vi) SEQ ID NOs: 18, or 30, or a sequence having 1-2 amino acid substitutions, deletions or additions of the sequence of SEQ ID NOs: 18, or 30.

43. The antibody of claim 41 comprising one CDR selected from the group consisting of

- SEQ ID NOs:15, or 27, and a sequence having 1-4 amino acid substitutions, deletions or additions of the sequence of SEQ ID NOs:15, or 27.

44. The antibody of claim 1 which is an intact antibody selected from the group consisting of: an intact IgG1 antibody, an intact IgG2 antibody, an intact IgG3 antibody, an intact IgG4 antibody, an intact IgM antibody, an intact IgA1 antibody, an intact IgA2 antibody, an intact secretory IgA antibody, an intact IgD antibody, and an intact IgE antibody, wherein the antibody is glycosylated in a eukaryotic cell.

45. The antibody of claim 1 which is an antibody fragment or a single chain antibody.

46. The antibody of claim 1 which is a binding-domain immunoglobulin fusion protein comprising (i) a binding domain polypeptide in the form of a heavy chain variable region or a light chain variable region that is fused to an immunoglobulin hinge region polypeptide, (ii) an immunoglobulin heavy chain CH2 constant region fused to the hinge region, and (iii) an immunoglobulin heavy chain CH3 constant region fused to the CH2 constant region, wherein the heavy chain variable region or light chain variable region comprise at least one human variable region selected from the group consisting of (a) SEQ ID NOs:2, 4, 6, 8, 10, or 12 and (b) a sequence which is at least 90% homologous to any one of the amino acid sequences as set forth in (a) above.

47. The antibody of claim 1 produced by a hybridoma which includes a B cell obtained from a transgenic non-human animal, in which V-(D)-J gene segment rearrangements have resulted in the formation of a functional human heavy chain transgene and a functional human light chain transgene, fused to an immortalized cell.

48. A hybridoma comprising a B cell obtained from a transgenic non-human animal in which V-(D)-J gene segment rearrangements have resulted in the formation of a functional human heavy chain transgene and a functional light chain transgene fused to an immortalized cell, wherein the hybridoma produces a detectable amount of the monoclonal antibody of claim 1.

49. A hybridoma which produces a human monoclonal antibody encoded by human IgG heavy chain and human kappa light chain nucleic acids comprising nucleotide sequences in their variable regions as set forth in SEQ ID NOs:1, 5, or 9 and SEQ ID NOs:3, 7, or 11, respectively, and conservative sequence modifications thereof.

50. A hybridoma which produces a human monoclonal having IgG heavy chain and kappa light chain variable regions which comprise the amino acid sequences as set forth in SEQ ID NOs:2, 6, or 10 and SEQ ID NOs: 4, 8, or 12, respectively, and conservative sequence modifications thereof.

51. The antibody of claim 1 produced by a transfectoma comprising nucleic acids encoding a human heavy chain and a human light chain.

52. A transfectoma comprising nucleic acids encoding a human heavy chain and a human light chain, wherein the transfectoma produces a detectable amount of the antibody of claim 1.

5 53. A transfectoma which produces a human monoclonal antibody encoded by human IgG heavy chain and human kappa light chain nucleic acids comprising nucleotide sequences in their variable regions as set forth in SEQ ID NOs:1, 5, or 9 and SEQ ID NOs:3, 7, or 11, respectively, and conservative sequence modifications thereof.

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54. A transfectoma which produces a human monoclonal antibody having IgG heavy chain and kappa light chain variable regions which comprise the amino acid sequences as set forth in SEQ ID NOs:2, 6, or 10 and SEQ ID NOs:4, 8, or 12, respectively, and conservative sequence modifications thereof.

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55. A eukaryotic or prokaryotic host cell which produces a human monoclonal antibody having heavy chain and light chain variable regions which comprise the amino acid sequences as set forth in SEQ ID NOs:2, 6, or 10 and SEQ ID NOs:4, 8, or 12, respectively, and conservative sequence modifications thereof.

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56. A transgenic non-human animal or plant which produces a human monoclonal antibody having heavy chain and light chain variable regions which comprise the amino acid sequences as set forth in SEQ ID NOs:2, 6, or 10 and SEQ ID NOs:4, 8, or 12, respectively, and conservative sequence modifications thereof.

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57. A method of producing a human monoclonal antibody which binds to human CD20, comprising:

30 immunizing a transgenic non-human animal having a genome comprising a human heavy chain transgene and a human light chain transgene with human CD20 or a cell expressing human CD20, such that antibodies are produced by B cells of the animal;

isolating B cells of the animal;

fusing the B cells with myeloma cells to form immortal, hybridoma cells that secrete human monoclonal antibodies specific for human CD20; and

35 isolating the human monoclonal antibodies specific for CD20 from the culture supernatant of the hybridoma, or the transfectoma derived from such hybridoma.

58. A method according to claim 57, wherein the immunization is performed with cells which have been transfected with human CD20.

59. A human monoclonal antibody which binds to human CD20
5 obtained by:
immunizing a transgenic non-human animal having a genome comprising a human heavy chain transgene and a human light chain transgene with a cell which has been transfected with human CD20, such that antibodies are produced by B cells of the animal;
10 isolating B cells of the animal;
fusing the B cells with myeloma cells to form immortal, hybridoma cells that secrete human monoclonal antibodies specific for human CD20; and
isolating the human monoclonal antibodies specific for CD20 from the culture supernatant of the hybridoma, or the transfectoma derived from such hybridoma.

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60. An isolated human antibody comprising a heavy chain variable region amino acid sequence derived from a human V_H3-13/DP-44 germline sequence (SEQ ID NO:54) and a light chain variable region amino acid sequence derived from a human V_L-L6/JK4-CK (SEQ ID NO:55) germline sequence, wherein the human
20 antibody binds to human CD20.

61. An isolated human antibody comprising a heavy chain variable region amino acid sequence derived from a human V_H3-09/JH6b germline sequence (SEQ ID NO:56) and a light chain variable region amino acid sequence derived from a
25 human V_L-L6/JK5 germline sequence (SEQ ID NO:57), wherein the human antibody binds to human CD20.

62. A composition comprising the human antibody of claim 1 and a pharmaceutically acceptable carrier.

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63. A composition comprising a combination of two or more human antibodies according to claim 1, which have complementary functional activities.

64. A composition comprising a first human antibody and a second human antibody, both of which bind to human CD20, wherein the first antibody has a human heavy chain and human kappa light chain variable regions comprising the amino acid sequences as set forth in SEQ ID NO:2 and SEQ ID NO:4, respectively, and conservative sequence modifications thereof, and wherein the second antibody has a human heavy chain and human kappa light chain variable regions comprising the amino acid sequences as set forth in SEQ ID NO:10 and SEQ ID NO:12, respectively, and conservative sequence modifications thereof.
65. A composition according to claim 62 further comprising a therapeutic agent.
66. The antibody according to claim 1, further comprising a chelator linker for attaching a radioisotope.
67. An immunoconjugate comprising an antibody according to claim 1 linked to a cytotoxic agent, a radioisotope, or a drug.
68. A bispecific molecule comprising an antibody according to claim 1 and a binding specificity for a human effector cell.
69. A bispecific molecule comprising an antibody according to claim 1 and a binding specificity for a human Fc receptor or a binding specificity for a T cell receptor, such as CD3.
70. A method of inhibiting growth of a cell expressing CD20, comprising contacting the cell with an effective amount of an antibody according to claim 1 such that the growth of the cell is inhibited.
71. A method of killing a cell expressing CD20, comprising contacting the cell with the antibody of claim 1, such that killing of the cell expressing CD20 occurs.
72. The method of claim 70, wherein the cell is a B lymphocyte or a tumor cell.

73. A method of treating or preventing a disease or disorder involving cells expressing CD20, comprising administering to a subject a human antibody according to claim 1, in an amount effective to treat or prevent the disease.

5 74. The method of claim 73, wherein the disease is a B cell lymphoma.

75. The method of claim 73, wherein the disease is B cell non-Hodgkin's lymphoma.

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76. The method of claim 73, wherein the disease is selected from the group consisting of precursor B cell lymphoblastic leukemia/lymphoma and mature B cell neoplasms, such as B cell chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL), B cell prolymphocytic leukemia, lymphoplasmacytic lymphoma, mantle cell lymphoma (MCL), follicular lymphoma (FL), cutaneous follicle center lymphoma, marginal zone B cell lymphoma (MALT type, nodal and splenic type), hairy cell leukemia, diffuse large B cell lymphoma, Burkitt's lymphoma, plasmacytoma, plasma cell myeloma, post-transplant lymphoproliferative disorder, Waldenström's macroglobulinemia, and anaplastic large-cell lymphoma (ALCL).

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77. The method of claim 76, wherein the disease is follicular lymphoma (FL).

78. The method of claim 76, wherein the disease is B cell chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL).

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79. The method of claim 73, wherein the disease is selected from the group consisting of lymphomatoid granulomatosis, primary effusion lymphoma, intravascular large B cell lymphoma, mediastinal large B cell lymphoma, heavy chain diseases (including γ , μ , and α disease), lymphomas induced by therapy with immunosuppressive agents, such as cyclosporine-induced lymphoma, and methotrexate-induced lymphoma.

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80. A method of treating or preventing an immune disease involving CD20 expressing immune cells, comprising administering to a subject the antibody of claim 1, in an amount effective to treat or prevent the immune disease.

5 81. The method of claim 80, wherein treatment includes the killing of B cells which produce antibodies against autoantigens.

82. The method of claim 73, wherein the disease or disorder is selected from the group consisting of psoriasis, psoriatic arthritis, dermatitis, systemic
10 scleroderma and sclerosis, inflammatory bowel disease (IBD), Crohn's disease, ulcerative colitis, respiratory distress syndrome, meningitis, encephalitis, uveitis, glomerulonephritis, eczema, asthma, atherosclerosis, leukocyte adhesion deficiency, multiple sclerosis, Raynaud's syndrome, Sjögren's syndrome, juvenile onset diabetes, Reiter's disease, Behçet's disease, immune complex nephritis, IgA nephropathy, IgM
15 polyneuropathies, immune-mediated thrombocytopenias, such as acute idiopathic thrombocytopenic purpura and chronic idiopathic thrombocytopenic purpura, hemolytic anemia, myasthenia gravis, lupus nephritis, systemic lupus erythematosus, rheumatoid arthritis (RA), atopic dermatitis, pemphigus, Graves' disease, Hashimoto's thyroiditis, Wegener's granulomatosis, Omenn's syndrome, chronic renal failure, acute infectious
20 mononucleosis, HIV, and herpes virus associated diseases.

83. The method of claim 82, wherein the autoimmune disease is rheumatoid arthritis (RA).

25 84. The method of claim 73, wherein the disease is an inflammatory, immune and/or autoimmune disorder selected from ulcerative colitis, Crohn's disease, juvenile onset diabetes, multiple sclerosis, immune-mediated thrombocytopenias, such as acute idiopathic thrombocytopenic purpura and chronic idiopathic thrombocytopenic purpura, hemolytic anemia, myasthenia gravis, systemic sclerosis, and pemphigus
30 vulgaris.

85. The method of claim 73, wherein the disease is an inflammatory, immune and/or autoimmune disorder selected from inflammatory bowel disease (IBD), ulcerative colitis, Crohn's disease, and multiple sclerosis.

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86. The method of claim 70, further comprising separately administering another therapeutic agent to the subject.

87. The method of claim 86, wherein the therapeutic agent is a cytotoxic agent or a radiotoxic agent.

88. The method of claim 86, wherein the therapeutic agent is an immunosuppressant.

89. The method of claim 86, wherein the therapeutic agent is an immunological modulating agent, such as a cytokine or a chemokine.

90. The method of claim 86, wherein the therapeutic agent is selected from the group consisting of doxorubicin, cisplatin, bleomycin, carmustine, chlorambucil, and cyclophosphamide.

91. The method of claim 86, wherein the therapeutic agent is selected from the group consisting of anti-CD25 antibodies, anti-CD19 antibodies, anti-CD21 antibodies, anti-CD22 antibodies, anti-CD37 antibodies, anti-CD38 antibodies, anti-IL6R antibodies, anti-IL8 antibodies, anti-IL15 antibodies, anti-IL15R antibodies, anti-CD4 antibodies, anti-CD11a antibodies, anti-alpha-4/beta-1 integrin (VLA4) antibodies, CTLA4-Ig, and anti-C3b(i) antibodies.

92. An *in vitro* method for detecting the presence of CD20 antigen, or a cell expressing CD20, in a sample comprising:
contacting the sample with the antibody of claim 1 under conditions that allow for formation of a complex between the antibody and CD20; and
detecting the formation of a complex.

93. A kit for detecting the presence of CD20 antigen, or a cell expressing CD20, in a sample comprising the antibody of claim 1.

94. An *in vivo* method for detecting CD20 antigen, or a cell expressing CD20, in a subject comprising:
administering the antibody of claim 1 under conditions that allow for formation of a complex between the antibody and CD20; and
detecting the formed complex.

95. An expression vector comprising a nucleotide sequence encoding the variable region of a light chain, heavy chain or both light and heavy chains of a human antibody which binds human CD20.

96. The expression vector of claim 95, further comprising a nucleotide sequence encoding the constant region of a light chain, heavy chain or both light and heavy chains of a human antibody which binds human CD20.

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97. An expression vector comprising a nucleotide sequence encoding a heavy chain variable region comprising a nucleotide selected from the group consisting of the nucleotide sequences as set forth in SEQ ID NOs: 1, 5, and 9, and a light variable region comprising a nucleotide sequence selected from the group consisting of the nucleotide sequences as set forth in SEQ ID NOs: 3, 7, and 11, and conservative modifications thereof.

98. An expression vector comprising a nucleotide sequence encoding a heavy chain variable region comprising an amino acid sequence selected from the group consisting of the amino acid sequences as set forth in SEQ ID NOs: 2, 6, and 10, and a light chain variable region comprising the amino acid sequence selected from the group consisting of the amino acid sequences as set forth in shown in SEQ ID NOs: 4, 8, and 12, and conservative sequence modifications thereof.

99. A pharmaceutical composition comprising the expression vector of claim 95 and a pharmaceutically acceptable carrier.

100. An anti-idiotypic antibody binding to an antibody of claim 1.

101. An anti-idiotypic antibody binding to 2F2, 11B8 or 7D8.

102. Use of an anti-idiotypic antibody of claim 100 for detecting the level of human monoclonal antibody against CD20 in a sample.